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Synchronous hybrid procedure combining interventional radiology and endoscopy for esophagogastric varices with large gastro-renal shunt

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Abstract

Successful treatment of esophagogastric varices (EGV) with giant portal-systemic shunt is challenging. To explore the feasibility and safety of a novel hybrid procedure involving interventional radiology and endoscopy in the same sitting.

Three cases clinically diagnosed to have decompensated cirrhosis and EGV with giant gastrorenal shunt (GRS) on contrast-enhanced computed tomography (CT) were included. The hybrid procedures included: indirect portography, hepatic vein pressure gradient (HVPG) measurement, HVPG-based partial splenic embolization (PSE), retrospective GRS balloon occlusion, endoscopic histoacryl injection (EHI), balloon catheter radiography and withdrawal. All the procedures were done in the same operation room. Main outcomes measurements included operation time, complications, and re-bleeding events.

Hybrid interventions were performed successfully in 3 cases with a mean operation time of 63.3 minutes without any major intra- and post-operation complications. No rebleeding occurred at 6-month follow-up.

Synchronous hybrid intervention combining radiology and endoscopy is feasible and safe for patients with EGV and giant GRS, preliminary study with limited cases deserves further exploration.

Abbreviations: BO = balloon occluded, BO-ESI = balloon occluded endoscopic sclerosant injection, BRTO = balloon-occluded retrograde transvenous obliteration, CT = contrast-enhanced computed tomography, DSA = digital signature algorithm, EGV = esophagogastric varices, EHI = endoscopic histoacryl injection, EOI = ethanolamine oleic acid mixed lipiodol, EV = esophageal varices, FHVP = free hepatic venous pressure, GRS = gastro-renal shunt, GV = gastric varices, HVPG = hepatic vein pressure gradient, PSE = partial splenic embolization, SO-EIS = endoscopic shunt injection sclerotherapy, TIPS = transjugular intrahepatic portosystemic shunt, WHVP = wedged hepatic venous pressure.

Keywords: endoscopy, esophagogastric varices, gastrorenal shunt, hybrid procedure, radiology

1. Introduction

Gastric varices (GV) are one of the challenging clinical problems in nearly one-third of patients with portal hypertension.[1] Although GV bleed less frequently than esophageal varices, it can be more severe or even fatal because of their large size and rapid blood flow inside the varices.[2] The mortality rate in patients with bleeding from gastric fundal varices ranges from 25% to 55%.[3] The risk of rebleeding is 35% to 90% after spontaneous remission, and can reach up to 89% even after successful endoscopic therapy.[4,5] Owing to the distinct anatomy and pathophysiology, GV receive blood supply from the portal

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New Methods and Materials: In clinical practice, patient with decompensated liver cirrhosis rarely have giant gastro-renal shunt. To conduct a case–control study is difficult. Most previous studies have combined BO with EHI. This study is the first of its kind to use PSE with BO-EHI and prove its feasibility and safety.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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system and drain into the systemic vein mostly via the left renal vein known as gastro-renal shunt (GRS).[6] The prevalence of GRS in GV is as high as 85%.[7] The current treatments for GV include medical therapy, endoscopic therapy, surgery, and radiological interventions including transjugular intrahepatic portosystemic shunt (TIPS) and balloon occluded retrograde transvenous obliteration (BRTO).[8] Endoscopic therapy for GV which includes band ligation, sclerotherapy, and histoacryl injection is considered as the preferred first-line treatment.[9] Scleroligation demonstrated a faster rate of eradication than band ligation and is comparable in cost and in adverse event and recurrence rates. Although some studies have confirmed the safety of sclerotherapy,[10,11] use of sclerotherapy for GV is not suitable because abundant blood supply and faster blood flow in the GV, and high risk of complications such as ulcer formation and bleeding during the process of sclerotherapy. In clinical practice, gastro-renal shunt >1 cm in diameter is defined as large GRS, in the presence of large GRS, sclerosing agent injected locally at the GV site has tendency to migrate into GRS and subsequently in to the systemic circulation resulting in pulmonary or systemic embolism.[12,13] Some studies have reported that the rates of pulmonary and cerebral embolism to be as high as 2% to 3%.[12,14]

A new technique for treating GV with GRS, known as balloon-occluded retrograde transvenous obliteration (BRTO), is a promising solution. BRTO is a procedure performed by an interventional radiologist that treats GV with sclerosants fully injected into varices through GRS after balloon occlusion of the shunt.[15] This method significantly decreased the prevalence of sclerosants migration and has been proved to be effective in controlling or preventing GV bleeding.[16] Unfortunately, increased portal venous pressure after occlusion of the large portosystemic venous shunt may lead to aggravation of the esophageal varices, hypertensive gastropathy, ascites or retrograde development of the thrombus into the portal system.[14,18,19] In addition, during BRTO, one cannot accurately select the vessels (inside and outside the gastric wall) to be embolized at the same time. Moreover, in BRTO, the dosage of sclerosing agent used is relatively large. To overcome this problem, the technique of endoscopic shunt injection sclerotherapy (SO-EIS) was developed in Japan which successfully treated a patient with BRTO refractory IGVs.[20] The most preferred sclerosant is 5% ethanolamine oleic acid mixed with lipiodol (EOI). However, EOI can induce hemolysis-induced kidney damage and increase liver and kidney toxicity, as well as exacerbate esophageal varices due to the increased portal pressure, thereby increasing the risk of rebleeding.

To overcome these shortcomings, attempts of simultaneous balloon occlusion and endoscopic therapy have been reported recently.[19–22] Balloon occluded endoscopic sclerosant injection (BO-ESI) achieves thrombosis of the GV under endoscopy safely with the shunt temporary occluded by the balloon. The advantage of this process is that the portal pressure will not increase significantly, and it will not permanently block the shunt. However, the endoscopic sclerotherapy works by causing inflammatory reaction of blood vessels leading to their occlusion which is not guaranteed by BO-ESI. Moreover, it also cannot avoid occurrence of ectopic varices.

One group had previously reported the results of combined procedure of interventional balloon occlusion followed by endoscopic HI injection in 11 cases, showing that this technique is feasible and may be potentially advantageous in these high-risk patients.[21] However, this strategy had some limitations, especially the need to shift the patient from digital signature algorithm (DSA)-room to endoscopy center and the waiting time of 1 to 2 days, which might induce the shift or migration of the balloon and possibly ineffective occlusion.

Therefore, integrated treatment is the key. To the best of our knowledge, there are no reports of hybridizing the x-ray guided balloon occlusion and EHI simultaneously in the same sitting. Since the hepatic vein pressure gradient (HVPG)-based partial splenic embolization (PSE) was already being carried out at our center for treating cirrhotic hypertensive variceal bleeding, we conducted this novel strategy of simultaneous HVPG-guided PSE and BO-EHI.

2. Materials and methods

The study was conducted in the local hospital. The study was approved by the ethical review committee of our Hospital (301hnll-2017-05). Written informed consent was obtained from all the patients or their relatives. Three consecutive patients clinically diagnosed to have decompensated liver cirrhosis with recurrent episodes of upper gastrointestinal bleeding due to esophagogastric varices (EGV) were enrolled due to the presence of giant GRS as demonstrated on contrast enhanced CT images.

2.1. Pre-procedure preparations

Pre-procedural assessment included clinical evaluation; laboratory tests, and 6 contrast-enhanced CT. Scan after admission to the hospital. All 3 cases were treated with proton pump inhibitors and somatostatin before the operation. One patient had gastrointestinal bleeding before operation and received 2 units of packed red blood cells and emergency surgery to stop the bleeding.

2.2. Hybrid procedures

All the interventional procedures were performed in the same DSA room equipped with Philips FD20 imaging system and endoscopic workstation (Fujinon 4450 series) to fulfill the requirements of simultaneous hybrid procedures involving radiological intervention and endoscopic therapy. According to the clinical condition of the patients, the following methods were adopted. HVPG measurement: The patients were placed in supine position and the right internal jugular or femoral veins were punctured. Using Seldinger technique, a 5.5F balloon catheter (Edwards) was placed in the right hepatic vein over the 180 cm long guide wire. Free hepatic venous pressure (FHVP) was measured by connecting the pressure sensor and accessories (Smith Medical). Wedged hepatic venous pressure (WHVP) was determined after inflating the balloon to the suitable size and occluding the blood flow of right hepatic vein. These pressures were measured thrice and the average value was obtained. If the difference in the pressure values of any 2 measurements was >1.0 mmHg, then the measurements were repeated until the difference became <1.0 mmHg. HVPG was recorded as WHVP-FHVP. HVPG guided PSE: Right femoral artery was cannulated using Seldinger technique. 5F Cobra or super-smooth Yashiro catheter was placed in the splenic artery. Spleen size and its vascular supply were determined based on the radiography of the main arterial trunk entering the spleen and the vessels near the splenic hilum. Microspheres embolization agents (Boston Scientific) with diameter of 100 to 300 μm were fully immersed within 160,000 unit gentamicin along with contrast medium in the ratio of 1:1. This mixture was slowly infused into the

Table 1

Previous reports on treatment of esophagogastric varices with large gastro-renal shunt.

No.	Author	Year	Case	Type of operation	Embolic agent	Complication	Number of complications	Effectiveness			Follow-up time, d
								Hemorrhage rate in 1 year (%)	Hemorrhage rate after 1 year (%)	Eradication rate of varicose veins (%)	
1	Thakeb (4)	1995	58	Endoscopy	H	PP	1	0		8.6	
2	Kanagawa (8)	1996	32	BRTO	EO	0	0	0	0	96.9	168
3	Roesch (7)	1998			B	AE					
4	Hamamoto (15)	1999	2	BR-EIH	H	0	0	0			5
5	Ninoi (9)	2005	78	BRTO		0		0	1.5		
6	Joo (6)	2007		Endoscopy							120
7	Caldwell (2)	2012		BRTO							
8	Sato (12)	2015	16	BRTO Endoscopy	S	0	0	0	0	38.3	
9	Wu (13)	2016	11	BR-EIH	H		0	0	0	91	228 ± 153
10	Hatanaka (14)	2017	1	BR-EIS	S		0	0	0		

AE = abnormal embolization, B = bucrylate, BR-EIH = balloon-occluded retrograde-endoscopic injection histoacryl, BR-EIS = balloon-occluded retrograde-endoscopic injection sclerosant, BRTO = balloon-occluded retrograde transvenous obliteration, EO = 5% ethanolamine oleate iopamidol, H = Histoacryl, PP = portal pyemia, S = sclerotherapy.

main trunk of splenic artery 7 under fluoroscopic guidance. One-third of total amount of the microspheres was given initially and angiogram was repeated. Additional microspheres were injected until the spleen developed speckled or fog-like appearance. Procedure was stopped once 40% to 50% of the arterial supply of the spleen was blocked. Post PSE HVPG remeasurement: Remeasurement was carried out with the same method as described previously. If the HVPG decreased by ≥20% from baseline, then the PSE stopped. If not, then 1/3 amount of the remaining microspheres were injected until the HVPG decreased by 20%. At the end of the procedure, the catheter and the sheath were withdrawn. Local compression hemostasis was achieved using sterile gauze bandage. BO-EHI: According to the BRTO procedure described by Kanagawa et al,[15] a balloon occlusive catheter was inserted into the GRS via the right femoral vein. Angiography was performed to evaluate the size and location of GV and GRS using balloon occlusion. GRS was occluded by a 5.5F or 7F Fogarty balloon. The diameter of the balloon was chosen according to the diameter of GRS which varied between 9 and 20 mm. Histoacryl was endoscopically injected into gastric varies, average 4 to 6 unit per injection, while the gastrorenal shunt was temporarily occluded with the balloon catheter. The balloon catheter was withdrawn under fluoroscopy guidance after endoscopic procedure.

2.3. Post procedure care

Antibiotics (second generation cephalosporins) were administrated for 3 to 7 days after the procedure. Proton pump inhibitors, somatostatin, glutathione supplements, and antipyretics were given for 1 week. No vasoactive drugs were used to prevent rebleeding after the operation. Patients could be discharged 1 week later once repeat endoscopy, contrast-enhanced computed tomography CT abdomen, and laboratory tests demonstrated no obvious perioperative complications and adverse events. The follow up was later continued every 3 to 6 months. Previous reports on treatment of esophagogastric varices with large gastro-renal shunt have been described inTable 1

3. Results

The demographic data, liver function, type of varices and GRS diameter of the 3 patients have been described in Table 2. None of these patients had underwent isolated endoscopic, medical, or radiological procedure before the hybrid procedure for variceal bleeding. We adopted the same hybrid procedure for the 3 patients. Three interventions (HVPG+PSE+BO-EHI) were performed successfully in the same operation room. The total procedure time for these patients was 45, 55, and 90 minutes respectively. The baseline HVPG was 12, 12, and 8 mmHg before PSE, and decreased to 10, 8, and 6 mmHg after PSE (mean decrease 2.67 mmHg, >20% vs baseline) (Table 3). One patient received endoscopic esophageal variceal ligation 1 week after the hybrid intervention. The mean hospital stay after the procedure was 8 days (range: 5–12 days). There were no moderate or severe complications except for mild abdominal pain for 3 to 5 days. The endoscopy examination showed shrinking of the varices in all the 3 patients 1 month after procedure with no bleeding. Three months after the intervention, the endoscopy examination showed complete resolution of the varices. At the mean follow up of 18 months, all the patients are doing well without bleeding, ectopic embolism, infection, abnormal liver function, and renal function.

4. Discussion

In this study, we successfully carried out hybrid procedure of balloon occlusion with simultaneous EHI in single DSA

Table 2

Clinical features of the 3 patients who underwent hybrid procedures.

No.	Sex (male/female)	Age, y	Cause of liver cirrhosis	Child-Pugh classification	Sarin classification of GV	GRS diameter, cm
1	Female	56	HBV infection	A	GOV2	0.6
2	Male	63	Alcohol	A	IGV	0.8
3	Female	58	HBV infection	A	IGV	1.0

GOV = gastroesophaged varices, GRS = gastro-renal shunt, GV = Gastric varices, HBV = hepatitis B virus, IGV = isolated gastric varices.

Table 3

Comparison of total surgery time and baseline.

No.	Sex (M/F)	Total surgery time, min	HVPG before PSE, mmHg	HVPG after PSE, mmHg
1	F	45	12	10
2	M	55	12	10
3	F	90	8	6

F = female, HVPG = hepatic vein pressure gradient, M = male, PSE = partial splenic embolization.

operation room for 3 cases with GRS. To the best of our knowledge, such simultaneous BO-EHI in same sitting has not been reported in the literature. All the 3 patients received the hybrid therapy successfully without any major complications and were discharged within 1 week. Direct injection of Histoacryl into GV may be accompanied by the potential serious complication of embolism in multiple organs. Balloon occlusion temporally achieves sufficient accumulation of Histoacryl in the GV during endoscopic injection, which may reduce the risk of sclerosant migration. Moreover, as Histoacryl is locally injected into the gastric fundal varices, it has little effect on portal system hemodynamics and hence minimal risk of esophageal varices or hypertensive gastritis. In the follow-up endoscopy, 1 patient underwent variceal banding for pre-existing esophageal 9 varices and there was no worsening of esophageal varices or portal hypertensive gastropathy. Histological glue is superior to sclerosing agent in the treatment of gastric varices. Sclerotherapy involves injection of sclerosant such as ethanolamine oleate, alcohol, or tetradecyl sulfate into varices. It is effective in treating esophageal varices, but it is associated with high rates of rebleeding and adverse events when used for GV1.[23] The reported time for keeping the balloon inflated varied from 40 minutes to 48 hours.[21,23] Prolonged closure of outflow tract affects GV pressure and has potential risk of thrombosis. In the present study, the catheter was left in place for about 24 hours after the endoscopic Histoacryl injection. In the study by Sato et al,[20] the time span of balloon occlusion was approximately 40 minutes while in Wu et al[21] study the time span was 36 to 48 hours.[22] This temporal occlusion does not change the hemodynamics of GV and GRS for much time and lowered the incidence of regional hypertension. However, BO-EHI procedure is technically challenging procedure and requires great expertise. Also, there was significant radiation exposure to the patients. Unlike the previous reports, we added HVPG guided PSE before BO-EHI. The reason being, in liver cirrhosis, there is splenomegaly, which is not only the result of portal hypertension, but also an important factor in promoting the progression of portal hypertension. The splenic vein is the largest branch of portal vein system, accounting for the majority of blood flow of portal vein. By doing PSE, we reduced the portal hypertension thereby decreasing the risk of rebleed. The follow up endoscopic examination at 6 months showed complete resolution, which may be partly due to the role of PSE in reducing pressure. During the 18-month follow-up, there was no recurrent bleeding, no relapse of GS, no deterioration of liver functions. The 18-month endoscopic follow-up showed eradiation of GVs without exacerbation of EV and portal gastropathy. No bleeding or rebleeding occurred 18 months post operation. In an ongoing observational study at our center, we have observed immediate reduction in HVPG by 20% from the baseline levels. The decrease in portal system pressure by PSE may favor the subsequent endoscopic operation and also hopefully benefit the patient from the rebleeding in the follow up period. There are several reports describing the combined use of PSE with endoscopy.[13] We believe that this method may be of some clinical 10 value, which is worth further exploring. The present study has several limitations. First, the present study was a case series. Second, it was a single-center study. Third, the duration of follow up was short. Future multicenter studies with larger sample size and long-term follow up are required to validate the findings of this study.

5. Conclusion

BO-EHI in combination with PSE is safe and effective in GV patients with large GRS. Future larger studies are required to determine its real potential.

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